PIEDMONT
ANIMAL HEALTH

Mr. Scott Pruitt
Administrator of the Environmental Protection Agency
Environmental Protection Agency
1101A
1200 Pennsylvania Avenue, N.W.
Washington, DC 20460
February 21, 2017

Dear Mr. Pruitt:

Our company, Piedmont Animal Health, has invented a safe green product that kills ticks (attached and unattached) very rapidly. In 2011 we received an EPA registration (86865-1) for this product (Resultix™) to kill ticks on dogs and cats. At that time one of the EPA personnel also mentioned that due to the safety of this product a human label would be possible. In the meantime Piedmont commissioned the USDA ARS Branch to conduct a unique study to evaluate a series of questions including the speed with which an attached tick stops feeding. The 2014 research findings indicated that at standard rates tick feeding is stopped immediately after a tick is sprayed. This finding is significant since transmission of disease is caused during tick feeding. After presenting this data to the EPA another meeting was scheduled in which the CDC participated as ticks transmit diseases. In the joint conversation with the EPA and CDC we were asked if ticks regurgitated after being treated with Resultix. Again Piedmont initiated a project with the USDA to answer this question but after attempting to evaluate regurgitation the researcher concluded that it was not possible to answer the question with current technology. Piedmont conveyed those results in 2016 to the EPA and requested a human label based upon answering the feeding question at which point we had a most unusual conversation. The EPA commented that since the CDC did not include spraying a tick in its protocol for handling ticks that it would be difficult for the EPA to label the product for humans.

Piedmont kindly requests some assistance from your office in expediting this matter. The EPA is the responsible agency as determined by the EPA and the protocol rationale noted makes no sense. As an example, prior to antibiotics limbs were cut off to prevent gangrene so any protocols prior to the advent of antibiotics were of course obsoleted by technology. To our knowledge there is no product registered in the US that is labeled to kill ticks on humans. It is our opinion that the EPA has intentionally delayed providing a human label because this will be a novel registration. It would be a shame if this safe and highly effective tick product couldn't be labeled for use on humans to benefit Americans in their battle with ticks. Piedmont is available to discuss the situation by phone or to meet you in person to discuss.

Thanks for all your effort on behalf of the USA.

Yours sincerely,

Roland Johnson,
Chairman and CEO
Piedmont Animal Health, LLC
Greensboro, NC 27410
rjohnson@piedmontpharma.com
336-580-1508

Michael Kelly
COO and CFO
mkelly@piedmontpharma.com
336-554-3602

Detailed Account of EPA Interactions to Add Humans to Resultix Label (October 24, 2014)

PAH emailed EPA on October 24, 2014 requesting a meeting to discuss adding humans to the label (Attachment 1). On November 9, 2014, a meeting for December 10, 2014 with EPA was scheduled. The meeting request and minutes from that meeting are Attachments 2 and 3. During the December meeting two things were discussed: the in vitro feeding study (Attachment 4) and jurisdiction. EPA was not sure if they actually had jurisdiction over a human use for killing ticks. Ms. Linda Hollis, Branch Chief for the Biopesticide Branch, said an internal meeting with the Office of General Counsel (OGC) would have to occur. On February 23, 2015, PAH was told a meeting was occurring and a response would be imminent. On April 29, 2015, PAH was told that a decision on jurisdiction had been made on April 7, 2015 but PAH had not been notified. EPA determined that Resultix® is a pesticide and under the jurisdiction of EPA. On April 30, 2015, PAH was given direction on how to proceed which included requesting a meeting. A meeting was requested (Attachment 5) and granted on May 4, 2015. Due to scheduling issues with EPA personnel the meeting was rescheduled to occur July 1, 2015. EPA, CDC and Piedmont were present for the phone conference. Piedmont was not informed that the CDC would be participating so Piedmont was not prepared to address concerns that CDC would present. The phone call did not address any questions that Piedmont had raised but introduced the CDC as another regulatory entity that had additional questions i.e. tick regurgitation and repellency that had never been presented during previous discussions.

After the July 1, 2015 meeting, Piedmont contacted the USDA Agricultural Research Services (ARS) in Beltsville, MD to discuss and possibly design another study to answer the regurgitation question. Dr. Andrew Li with additional resources provided by PAH conducted additional work in hopes of addressing the additional concerns. Dr. Li was able to determine that Resultix® did demonstrate some repellency. However after many attempts working with feeding ticks, it could not be determined if ticks would regurgitate gut contents once feeding was stopped and subsequent tick death ensued. On August 17, 2015, Piedmont was contacted by EPA stating that the request for guidance with regard to the data generated from the July 1, 2015 meeting was being considered. On November 16, 2015, the Branch Chief took over communications with Piedmont from Project Management. Any further inquiries about this project were to be directed to her. On January 8, 2016, Piedmont sent an email (Attachment 6) outlining the past history and requesting the minutes from the July 1, 2015 meeting. An email (Attachment 7) was sent August 3, 2016 to Sherada Hobgood, Ombudsman in the Pesticide Branch, in hopes of contacting someone to discuss the supplement approval. On August 29, 2016, Piedmont received a response (Attachment 8) from the meeting held December 10, 2014 which was prompted by an email sent January 8, 2016. On September 14, 2016, EPA scheduled a teleconference with PAH for September 28, 2016 from 10-11am (Attachment 9). On September 28, 2016 at 10:15 am, Piedmont received an email from EPA stating that they were having technical difficulties getting on the conference call the EPA had arranged. EPA apologized and rescheduled the meeting for October 25, 2016 at 12:30 pm. During this teleconference the Branch Chief stated that there needed to be a meeting between the liaison to CDC and EPA. PAH should email the Branch Chief reminding her that this meeting needs to occur. The following dates are follow-up requests to the Branch Chief reminding her about the liaison meeting: October 31, 2016, November 11, 2016, November 17, 2016, December 15, 2016 and January 19, 2017. On January 18, 2017, EPA communicated via phone call to inform Piedmont that there is no information that can be shared at this time.

Listing of Enclosures to the Letter

Attachment 1: Supplemental Label for Resultix® with human addition highlighted

Attachment 2: Agenda for December 10, 2014 Meeting

Attachment 3: Submission on January 16, 2015 of December 10, 2014 Meeting Minutes

Attachment 4: In-vitro Tick Study Report and Abstract from conference July 11-14, 2015

Attachment 5: Agenda for July 1, 2015 Meeting

Attachment 6: January 8, 2016 email requesting formal response from July 1, 2015 Meeting

Attachment 7: August 3, 2016 email to Sherada Hobgood requesting Ombudsman assistance

Attachment 8: August 29, 2016 response from EPA to the December 10, 2014 meeting

Attachment 9: Agenda for September 28, 2016 Meeting

FRONT PANEL

RESULTIX™

Kills Ticks on Dogs, Cats and Humans

ACTIVE INGREDIENT	
Isopropyl Myristate	50.0%
OTHER INGREDIENT	50.0%
TOTAL	100.0%

KEEP OUT OF REACH OF CHILDREN

CAUTION

See Side/Back Panel for First Aid

STOP - READ LABEL BEFORE USE

EPA Reg. No. 86865-1

EPA Est. No. 71979-SC-001

Manufactured for
Piedmont Animal Health LLC
204 Muirs Chapel Road, Suite 200
Greensboro, NC 27410

NET CONTENTS
20 mL (0.65 oz.)

SIDE PANEL

FIRST AID

If on skin:	• Take off contaminated clothing. • Rinse skin immediately with plenty of water for 15-20 minutes. • Call a poison control center or doctor immediately for treatment advice.
If in eyes:	• Hold eye open and rinse slowly and gently with water for 15-20 minutes. • Remove contact lenses, if present, after the first 5 minutes, then continue rinsing. • Call a poison control center or doctor immediately for treatment advice.
If inhaled:	• Move person to fresh air. • If person is not breathing, call 911 or an ambulance; then give artificial respiration, preferably mouth-to-mouth if possible. • Call a poison control center or doctor immediately for treatment advice.
If swallowed:	• Call a poison control center or doctor immediately for treatment advice. • Have person sip a glass of water if able to swallow. • Do not induce vomiting unless told to do so by a poison control center or doctor. • Do not give anything by mouth to an unconscious person.

HOT LINE NUMBER

Have the product container or label with you when calling a poison control center or doctor or going for treatment. You may also contact 1-800-222-1222 (American Association of Poison Control Centers) any time day or night for emergency medical treatment information. For medical emergencies call 1-800-422-9874. For customer questions call 1-800-255-6826.

PRECAUTIONARY STATEMENTS

HAZARDS TO HUMANS AND DOMESTIC ANIMALS

CAUTION. May cause dermal and eye irritation. Avoid contact with skin, eyes, or clothing. Wash thoroughly with soap and water after handling and before eating, drinking, chewing gum, using tobacco, or using the toilet.

ENVIRONMENTAL HAZARDS

This pesticide is toxic to invertebrates and fish. Do not discharge this product into lakes, streams, ponds, estuaries, oceans, or other waters where aquatic invertebrates or fish may be found.

BACK PANEL

DIRECTIONS FOR USE

It is a violation of Federal law to use this product in a manner inconsistent with its labeling.

RESULTIX™, when used as instructed below, will dissolve the outer wax layer coving the hard shell (cuticle) of the tick resulting in uncontrollable water loss and death of the tick. The tick stops feeding immediately when sprayed with Resultix.

For the removal and killing of attached and crawling ticks on dogs, cats and humans.

APPLICATION AND USE INSTRUCTIONS

For external use only.

Do not use near dog's, cat's or human's eyes.

Do not use on irritated skin.

Stop treatment with this product and consult a veterinarian or medical doctor if skin irritation or skin infection develops during use of product.

- Use when you see a tick or ticks on you, your dog or cat.
- Remove cap and hold bottle upright. Direct nozzle at tick and spray until tick is covered with solution (2 sprays).
- The tick once sprayed stops feeding immediately
- The tick will be dead within 3 hours; it will fall off of you, your dog or cat or will be immobile when removed.
- If tick falls off indoors within 3 hours of application, carefully pick up and dispose of tick using gloves or tweezers.
- After 3 hours, if the tick has not fallen off, remove carefully with gloves or tweezers and dispose of tick.
- Dispose of ticks by placing in sealable plastic bag, sealing the bag, and placing it in an outdoor garbage can.
- Wash hands after accidental exposure to any ticks.

STORAGE AND DISPOSAL

Do not contaminate water, food, or feed by storage and disposal.

Pesticide Storage:

Store in a dry place away from extreme heat and cold (tightly closed between 59° F – 86° F (15° C – 30° C). Keep container closed when not in use. Always store pesticide in the original container. Store away from food and pet food. Keep away from open flames.

In case of fire or other emergency, report at once by toll-free telephone to CHEMTREC (800-424-9300).

Pesticide Disposal and Container Handling:

Nonrefillable container. Do not reuse or refill this container.
When empty: place in trash or offer for recycling if available.
Never place unused product down any indoor or outdoor drain.

NOTICE: Seller warrants that the product conforms to its chemical description and is reasonably fit for the purposes stated on the label when used in accordance with directions under normal conditions of use. To the extent permitted by applicable law, this warranty or any other warranty of merchantability or fitness for a particular purpose, express or implied, does not extend to the use of this product contrary to label instructions, or under abnormal conditions, or under conditions not reasonably foreseeable to Seller. To the extent permitted by applicable law, buyer assumes the risk of any such use.

ANY PANEL (Do not substitute these for required statements)

Label Claims (one or more in various combinations, located in various places throughout the box and bottle/insert labels)

Breakthrough in tick killing for attached and crawling ticks

Convenient and easy to apply

For the Killing of Ticks on Dogs, Cats and Humans

Free of conventional pesticides

Patented spray formula once sprayed on the tick stops tick feeding immediately and softens the waterproof outer waxy layer of the tick's body causing dehydration

Direct spray formula is safe to use on humans and pets

Can be used as often as needed

Can be part of your tick prevention regimen

Tick Killing Solution™

Attachment 2

AGENDA

Tentative Dates for Meeting

Week of November 17-22, 2014
10-11 am

Piedmont Animal Health Attendees

Douglas I. Hepler, Ph.D.
Kathleen G. Palma, Ph.D.-Contact Person
Andrew Li, Ph.D.

Biopesticides and Pollution Prevention Division Attendees

Leonard S. Cole, Jr., Senior Regulatory Specialist
Clara Fuentes, Ph.D., Entomologist
Linda Hollis, Branch Chief

Meeting Background

Resultix® (86865-1) was approved August 25, 2011 as a spray to kill ticks found on cats and dogs. Since this approval Piedmont Animal Health has been working with the Agency to amend the existing label to include humans. This would be an amendment to an existing label with data supporting the mode of action of Resultix on attached, feeding ticks.

A protocol was submitted and reviewed in 2013. Dr. Andrew Li, an ARS researcher in Beltsville, MD incorporated some of the comments provided into the protocol. This protocol was used to collect data that will be presented at this meeting. Below are some findings that were noted and will be included in more detail in the final study report.

The tick used in this study was *Amblyomma americanum*, the lone star tick. *Ixodes scapularis*, the blacklegged tick would not attach to the silicone membrane. The ticks were fed on a silicone membrane system where tick feeding and respiration were monitored.

When Resultix was sprayed with less than the labeled rate tick feeding was blocked and tick respiration was abolished. The ticks died rapidly but did not detach. If the tick has not been attached for 24 hours, pathogen transmission can be reduced using this spray.

The revised label that Piedmont Animal Health would like to discuss is as follows:

Resultix Spray kills crawling and attached ticks found on cats, dogs and humans and stops feeding and respiration reducing transmission of pathogens associated with tick feeding.

Piedmont Animal Health respectfully requests a meeting to discuss this research and present the data found in the final study report.

Contact Information:

Kathleen (Kathy) G. Palma, Ph.D.
204 Muirs Chapel Road
Suite 200
Greensboro, NC 27410

kathy.palma@piedmontpharma.com
(b) (6) (cell)

If there are any questions concerning this submission, please contact me at 336-544-0320 x 202 or (b) (6) (cell).

Sincerely,

Kathleen G. Palma, Ph.D.
Vice President of Research and Development, Regulatory

Enclosure
- Minutes
- RESULTIX™ label
- MOU 225-73-8010
- Piedmont-ARS Report

Attachment 4

Piedmont-ARS MTA Work

Progress Report #2

Summary of biological data *(Table 2):* Compared to female ticks fed on live host (cattle), females attached to silicone membrane fed for longer time to reach repletion. Both the mean body weight of engorged females and egg masses they produced were significantly smaller than those fed on cattle. The female-to-egg mass conversion efficient index (CEI) for the membrane-fed females was half of those fed on cattle.

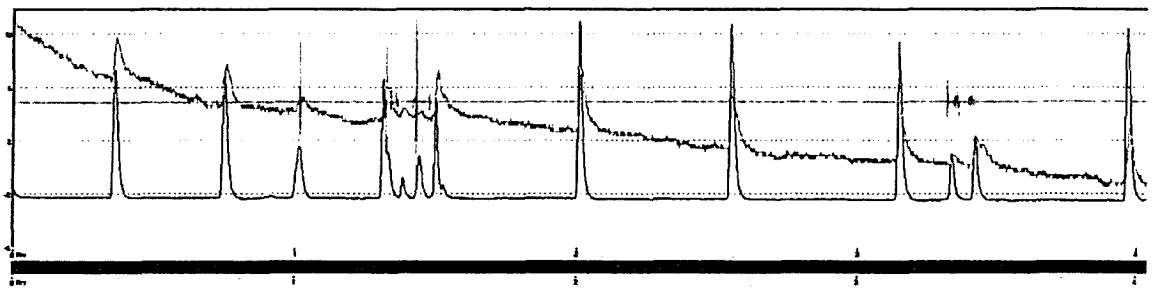
Table 2.

Feeding		Feeding	duration (d)		Body	weight (mg)		Egg mass	weight (mg)			CEI	
condition	n	mean	stdev	stderr	mean	stdev	stderr	mean	stdev	stderr	mean	stdev	stderr
in vivo (cattle)	35	11.7	1.0	0.2	754.0	148.0	25.0	458.0	141.0	34.0	60.5	15.2	2.6
in vitro (Membrane)	32	15.3	5.5	1.0	443.9	140.2	24.8	140.9	54.7	9.7	31.4	6.5	1.2

2. Effects of topical treatment of females attached to membrane with different doses of the test material (Resultix) on tick detachment and mortality

Adult males and females were placed into the feeders (5 to 8 pairs / feeder) to allow attachment to the silicone membrane. Attachment rate was checked 24 h later. We observed that attachment rate at 24 h was not high enough. So, we decided to wait for another 24 h, when attachment rate was uniformly high, before treating female ticks with test material. Feeding units were assigned into five (5) groups, each with a similar number (~ 15 – 20) of attached females. The five treatment groups were: (1) untreated control, (2) 0.5 µl of Resultix / tick, (3) 1.0 µl of Resultix / tick, (4) 2.0 µl of Resultix / tick, and (5) 4.0 µl of Resultix / tick.

In a preliminary test, ticks were observed every 5 min for a period of 60 min for detachment after treatment with Resultix. None of the treated ticks detached from membrane (data not shown). In subsequent experiments, ticks were examined under a dissection microscope at 30 min and 60 min after treatment. Live ticks that were attached to membrane and feeding always showed leg movements when being touched with a fine brush. Ticks that did not show such behavior were classified as "dead". Ticks were removed from membrane at 5 h post-treatment and were examined immediately under a microscope to determine mortality. A similar examination of the same ticks kept individually in small glass vials was also conducted at 24 to get final mortality data. Ticks were rated as "dead" when they failed to move their legs after being probed. Tick mortality was evident at 5 h and 24 h post-treatment when tick's color turned darker. Females in control groups were allowed to remain attached to membrane for the leg movement testing with a fine brush. All females in the control group were fed to repletion. The experiment was repeated two more times, so the final data set included three replicates for each treatment. Mortality data at different time post-treatment in each of five treatment groups was analyzed to generate mean mortalities. Two higher doses (8 and 16 µl / tick) were also tested later. These results are summarized in Tables 3, 4, and 5 (next page).

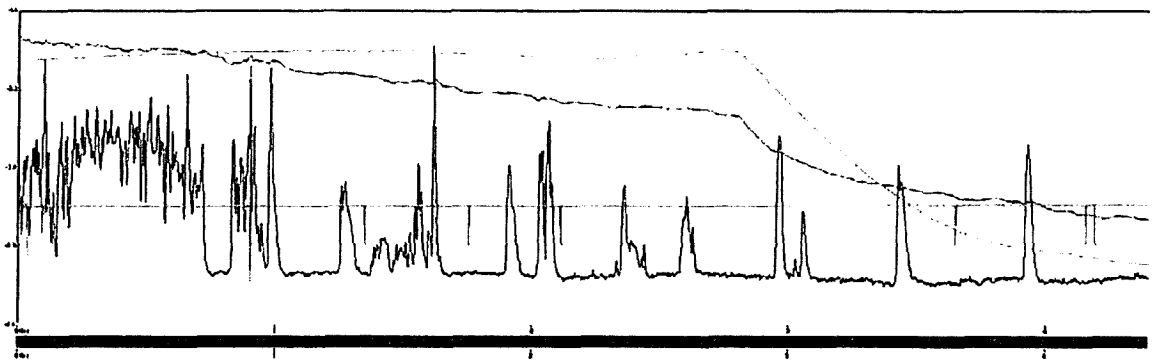


(2) Changes in tick respiration after treatment with Resultix.

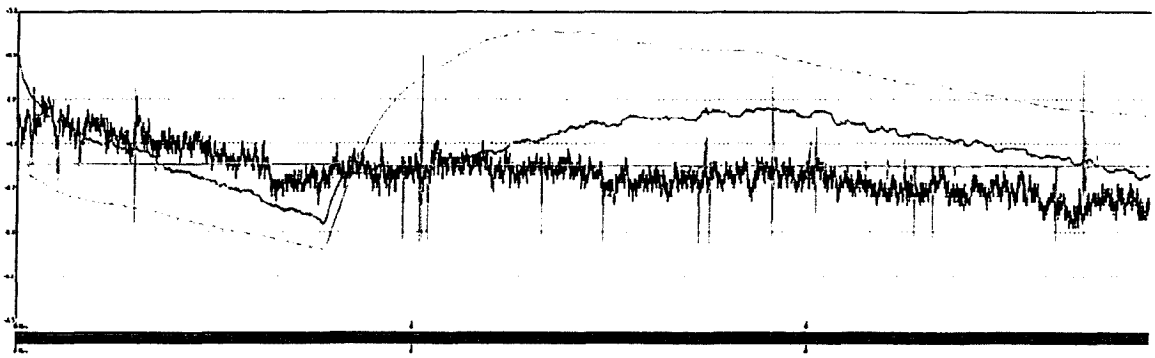
Over 30 adult females of *A. americanum*, including both unfed females and female partially fed on membrane, were used in this part of the study. Each individual female was recorded for several hours first to obtain regular activity pattern. Then, the tick was removed from the recording chamber and treated with a small dose of Resultix (0.19, 0.25, 0.5, 1, or 2 µl / tick) before being placed back into the chamber. The followings are results of physiological recordings that represent typical responses of ticks to Resultix treatment:

Preparation #1: *unfed female tick treated with 0.19 µl of Resultix*

- Before treatment

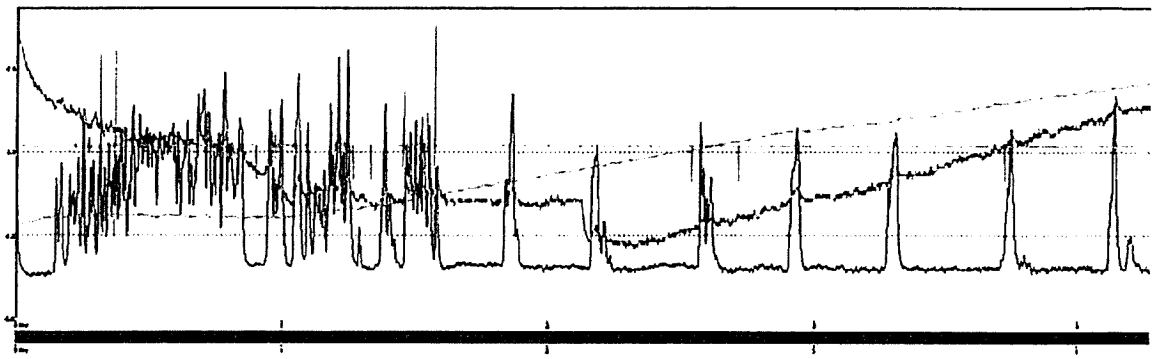


- After treatment (CO_2 peaks are gone, no significant water loss)

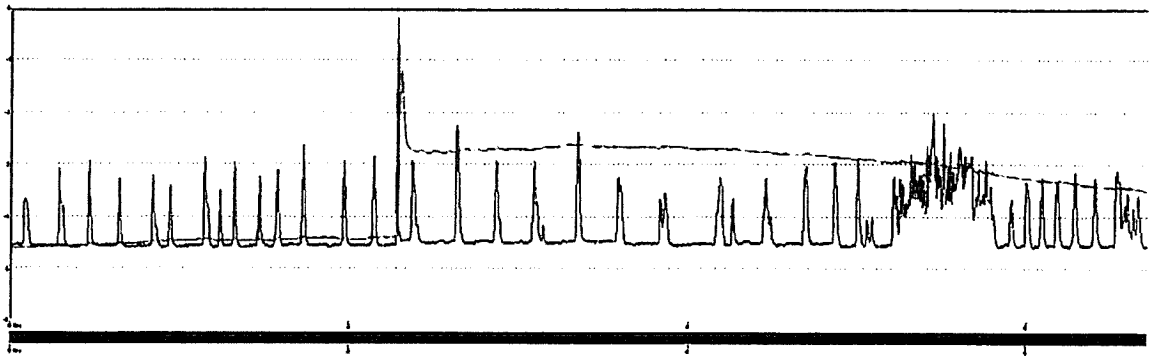


Preparation #3: *unfed female tick treated with 0.25 µl of Resultix*

- Before treatment

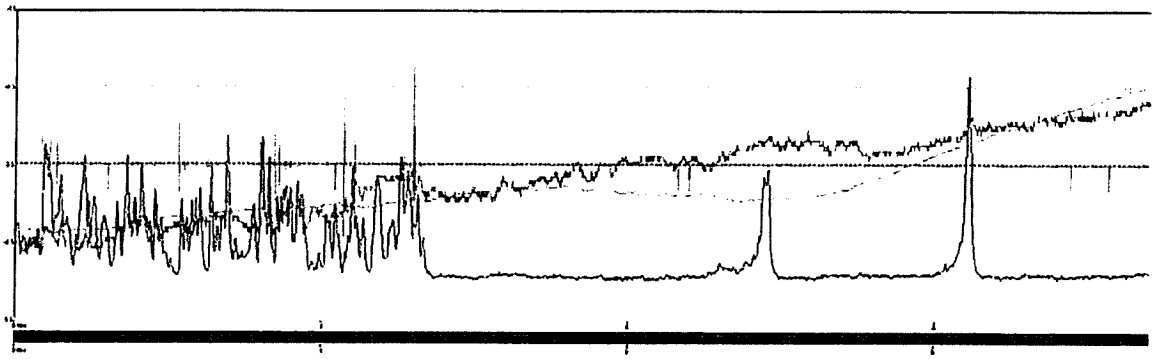


- After (CO_2 pattern was not affected ,shows signs of major water loss)

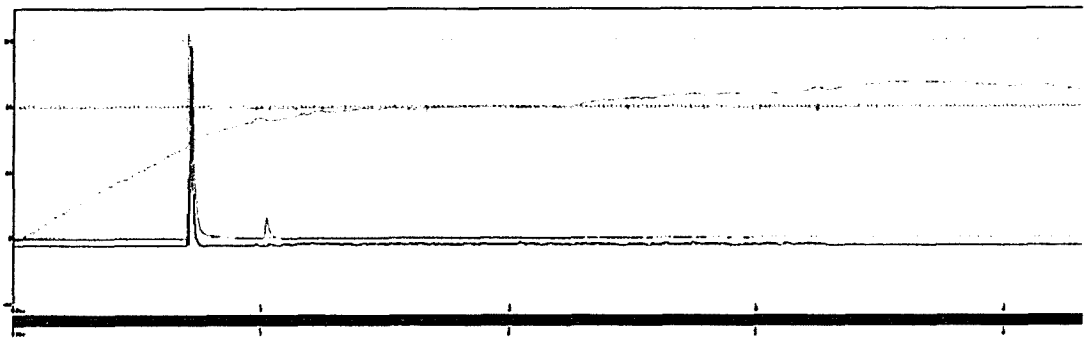


Preparation #4: *unfed female tick treated with 0.5 µl of Resultix*

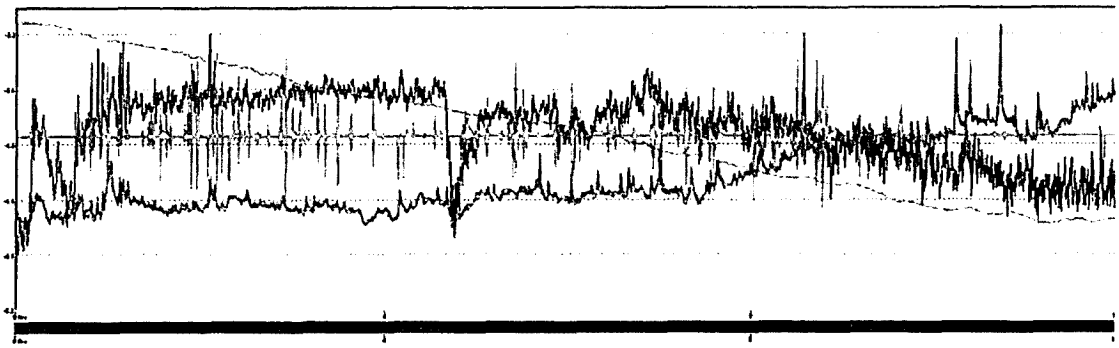
- Before treatment



- After treatment (CO_2 peaks are gone, shows sign of water loss)

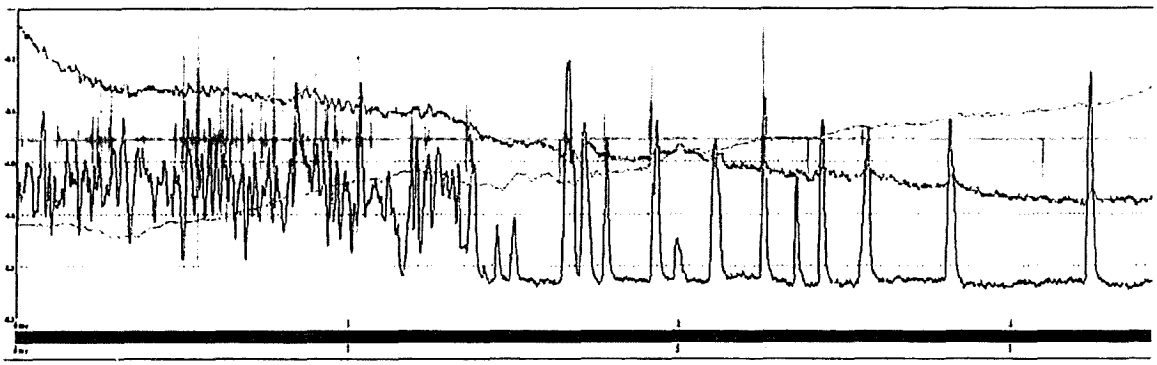


-Details

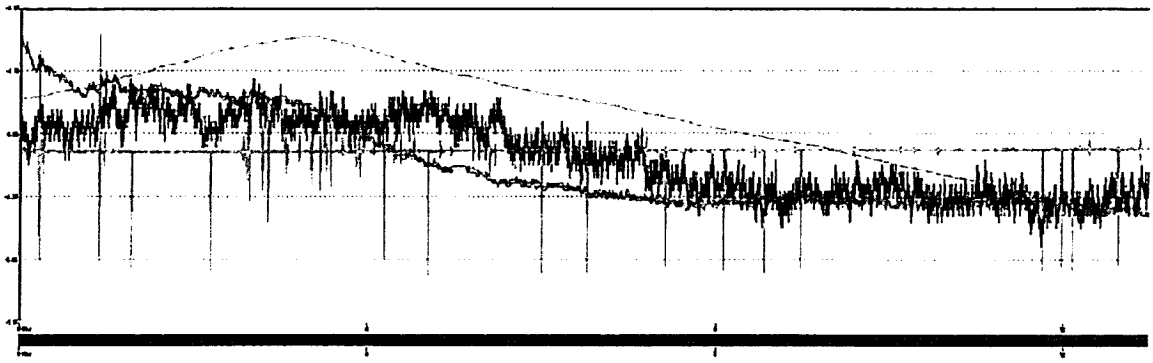


Preparation #5: *unfed female tick treated with 1.0 µl of Resultix*

- Before treatment

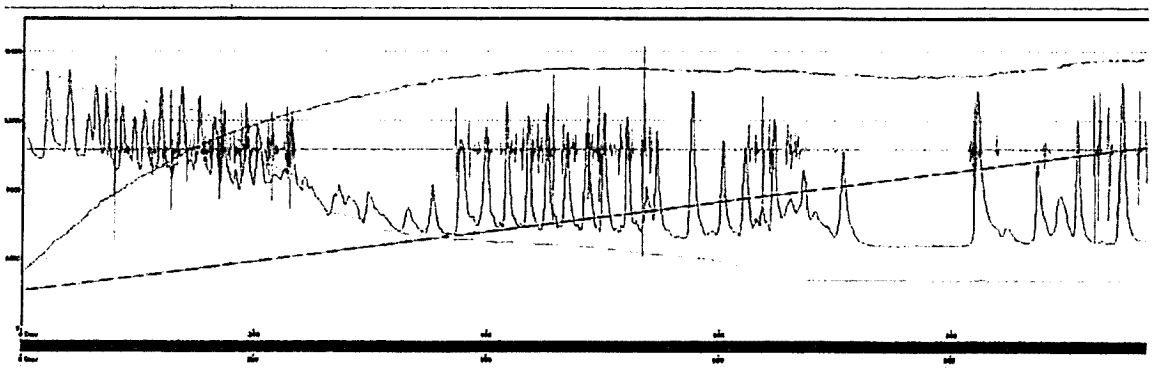


- After treatment (regular CO_2 peaks are gone, no sign of water loss)

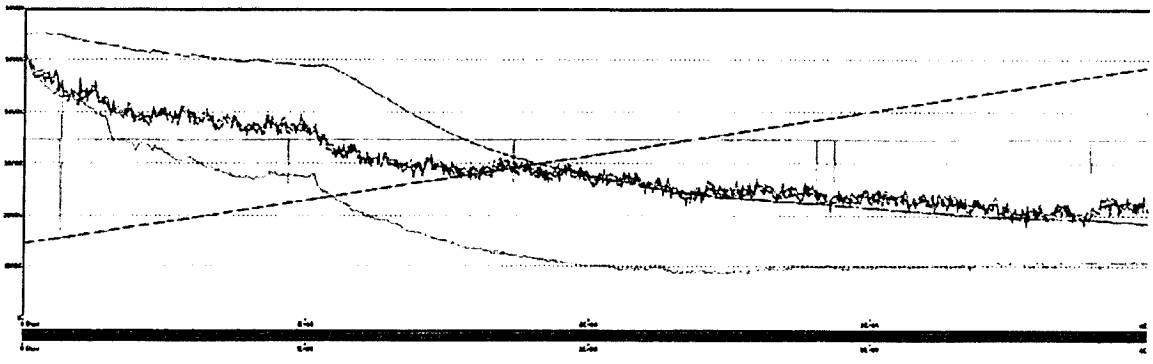


Preparation #6: *Membrane-fed female tick treated with 2.0 µl of Resultix*

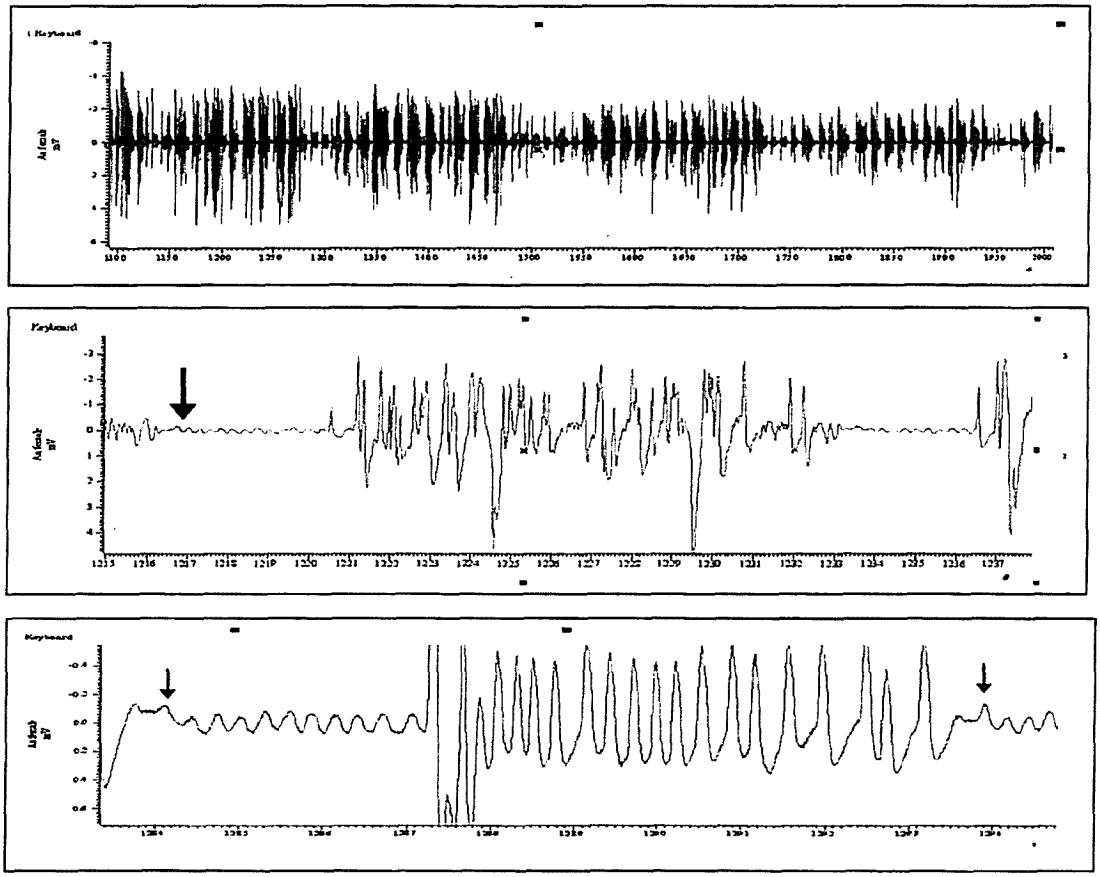
- Before treatment



- Post treatment (CO_2 peaks are gone, no sign of water loss)



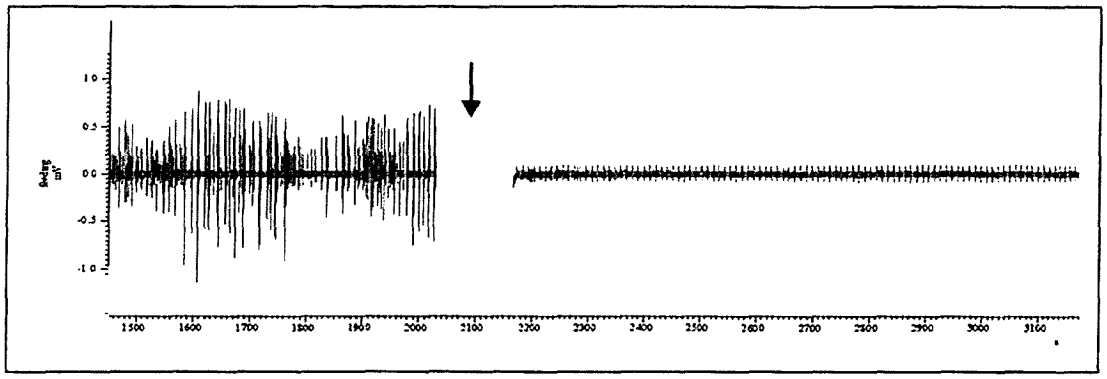
Preparation #2: The small units are blood ingestion activities, large units are salivation and/or movements of chelicerae during blood feeding.



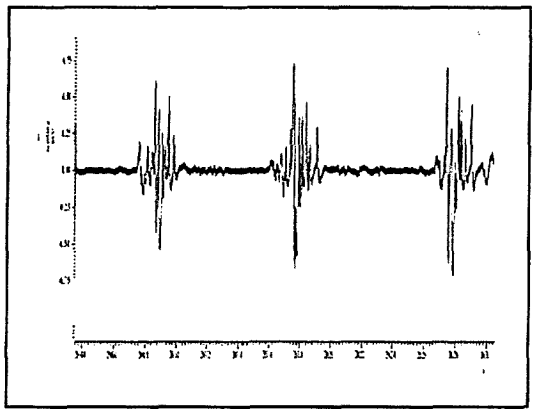
(2) Effects of Resultix treatment of blood feeding patterns of females attached to and feeding through membrane.

Preparation #1:

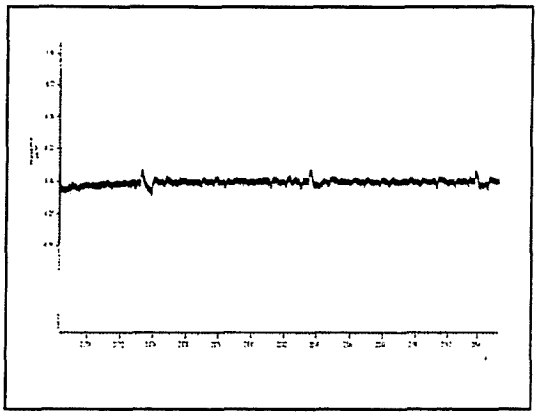
This female has fed on membrane for 4 days. It demonstrated normal rhythmic feeding patterns before treatment. Application of 1 µl of Resultix stopped feeding activities immediately.



- Before treatment

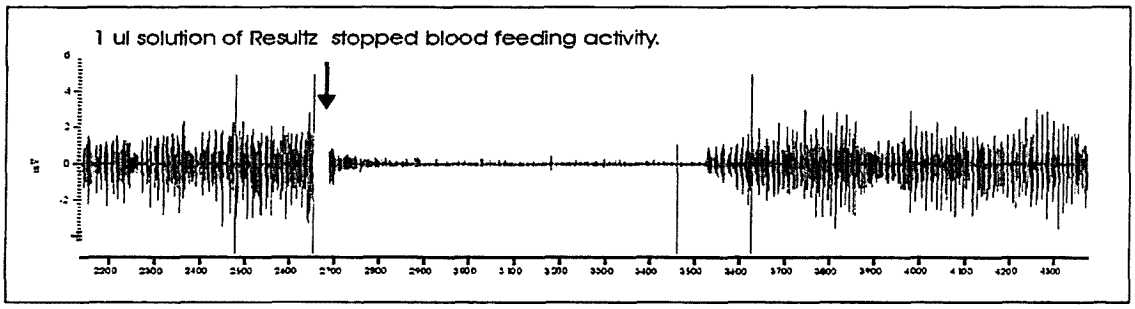


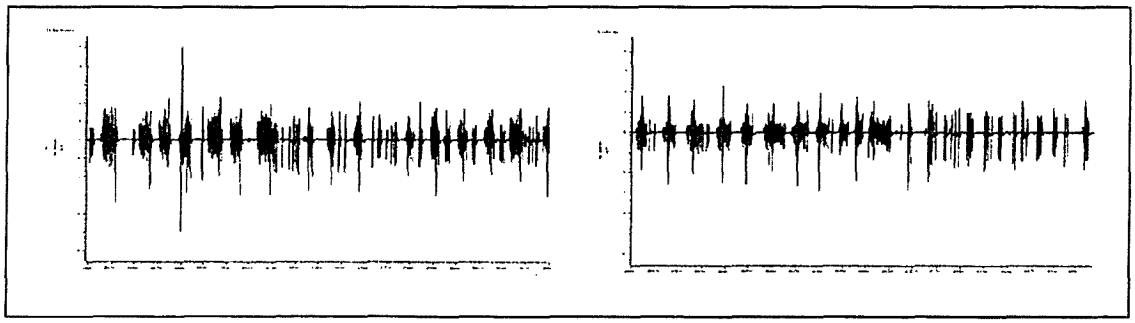
- After treatment

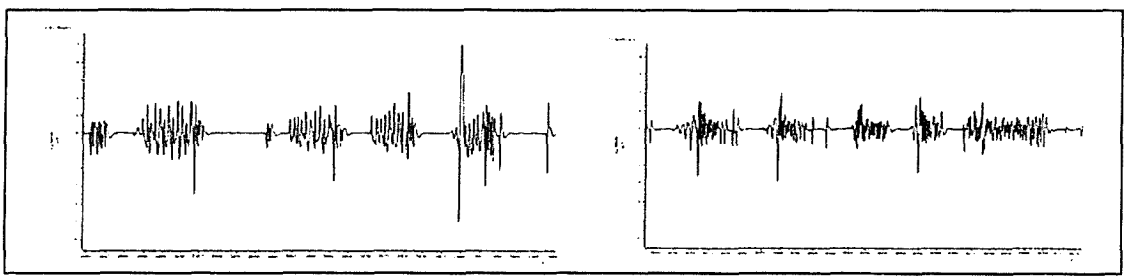


Preparation #2:

This female has fed on membrane for 2 days. It demonstrated normal rhythmic feeding patterns before treatment. Application of 1 µl of Resultix stopped feeding activities. However, feeding patterns recovered after 15 minutes.

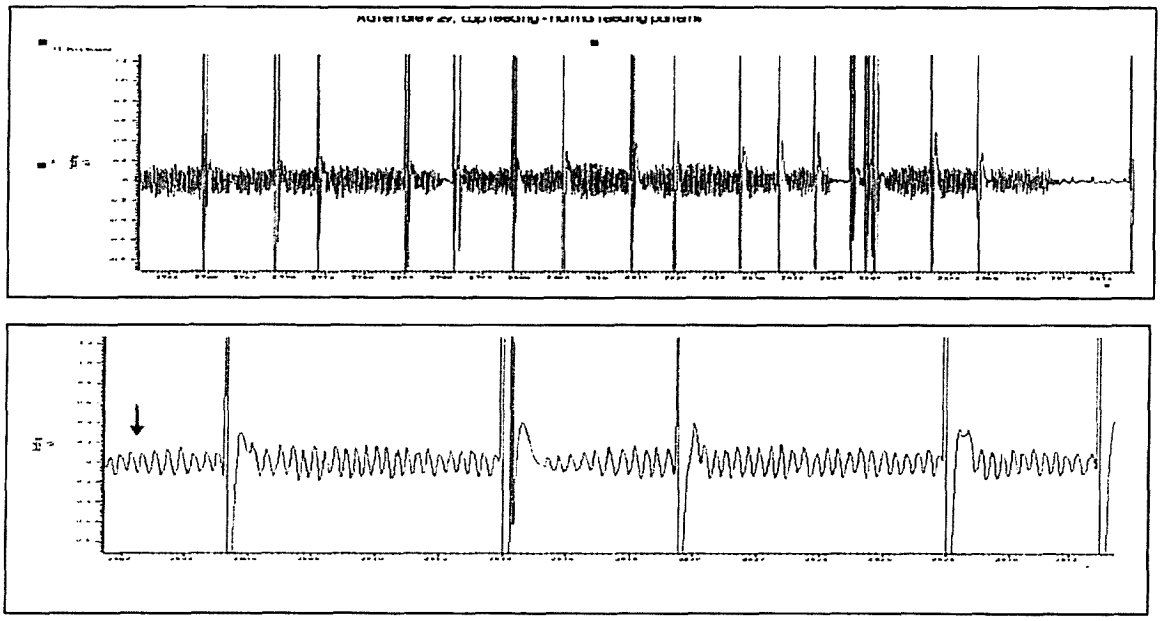






(3) Blood feeding pattern for female ticks fed blood through a capillary tube.

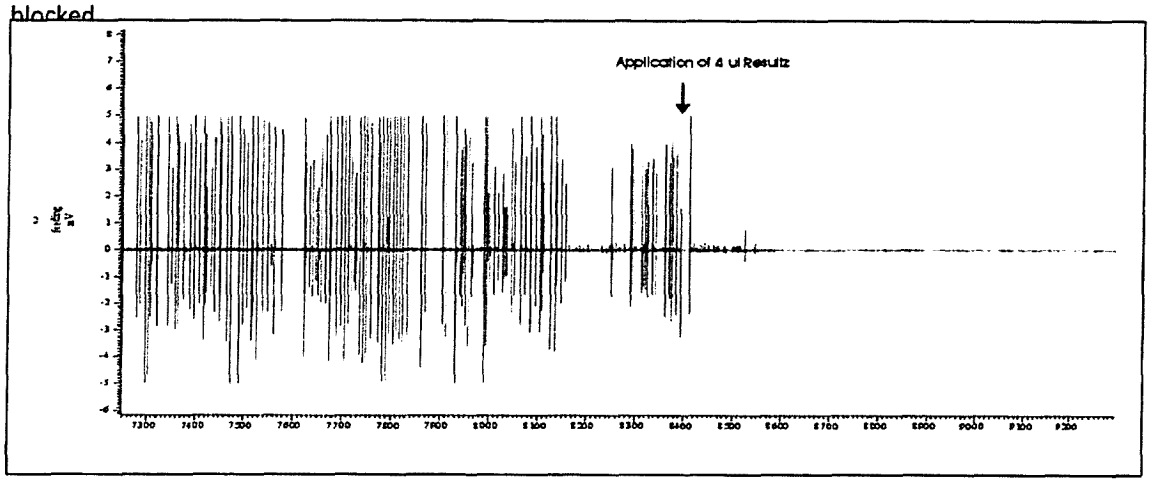
Compared to those from ticks fed blood through silicone membrane, the feeding patterns recorded from females fed through a micro capillary tube were clear and easy to interpret. The small peaks representing blood ingestion are easier to recognize, and there were fewer large spikes associated with salivation or movement of chelicerae. This is because blood was readily available and easy for tick to ingest with little or no resistance. The rate of blood ingestion was about 3 suctions / second.



(4) Effects of treatment of ticks with Resultix on blood feeding patterns of females that were fed through a micro capillary tube.

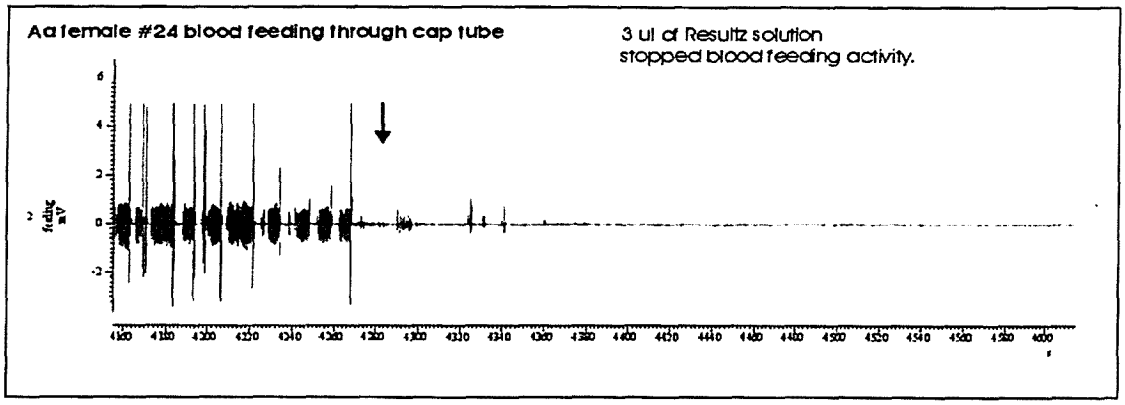
Preparation #1.

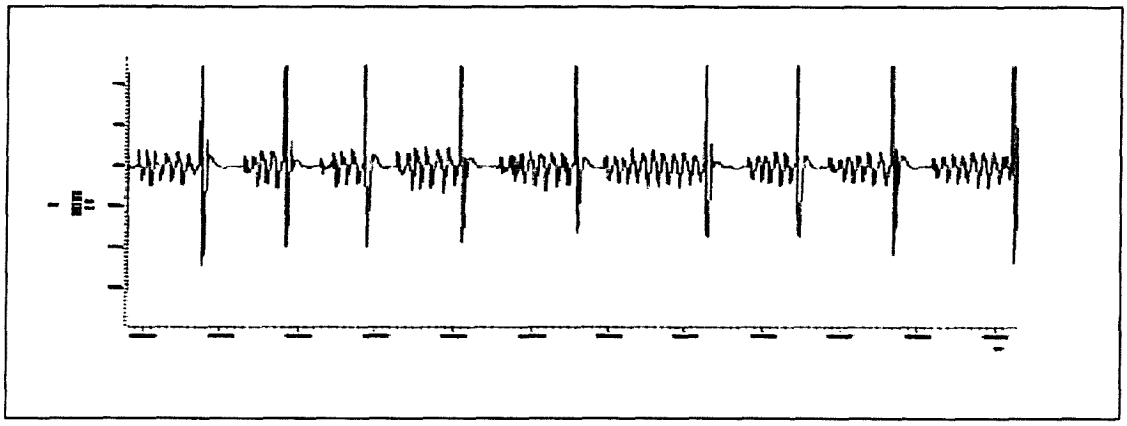
The tick described above was treated with 4 µl of Resultix. Feeding activity was immediately blocked.

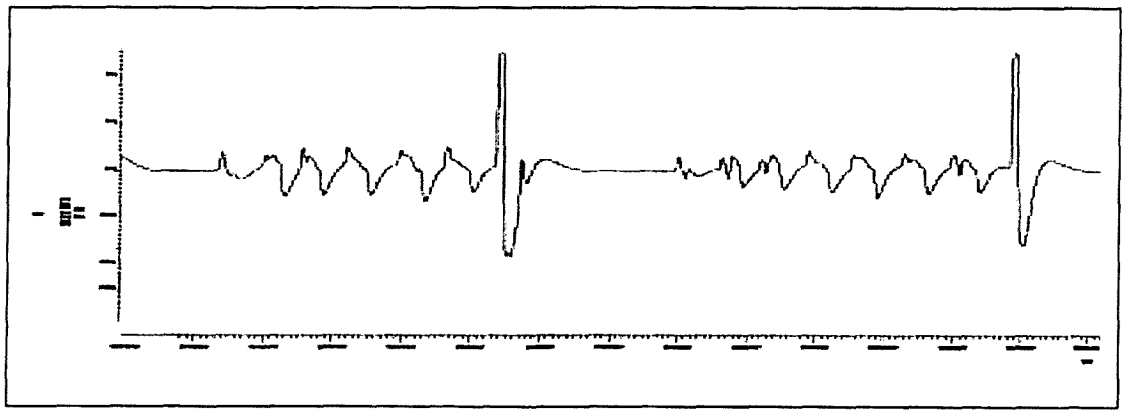


Preparation #2.

The tick showed normal regular ingestion pattern without much indication of salivation or cheliceral movement. Application of 3 µl of Resultix immediately blocked the tick feeding activity.

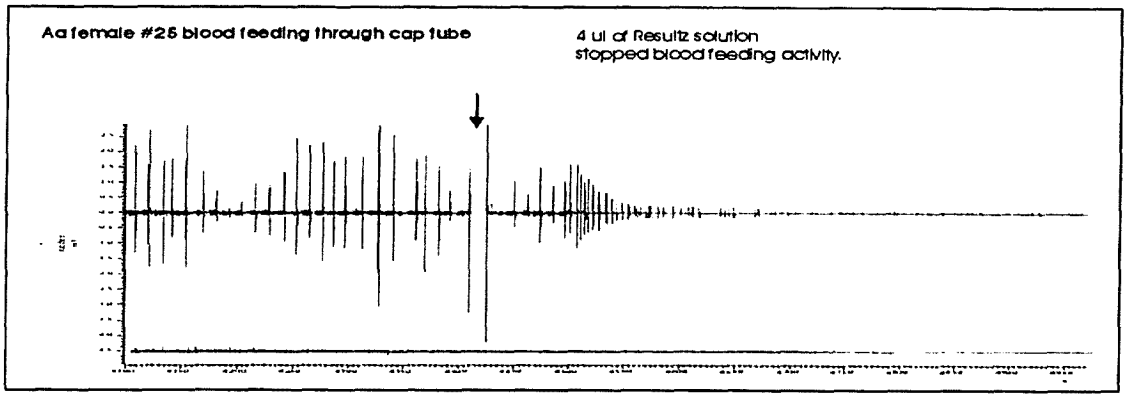




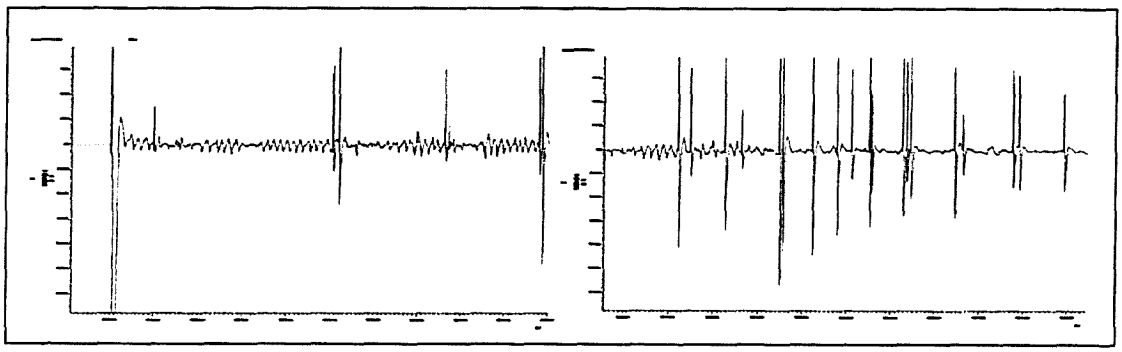


Preparation #3.

Application of 4 µl of Resultix also stopped feeding activities (in 2 min) of the third female fed through capillary tube.

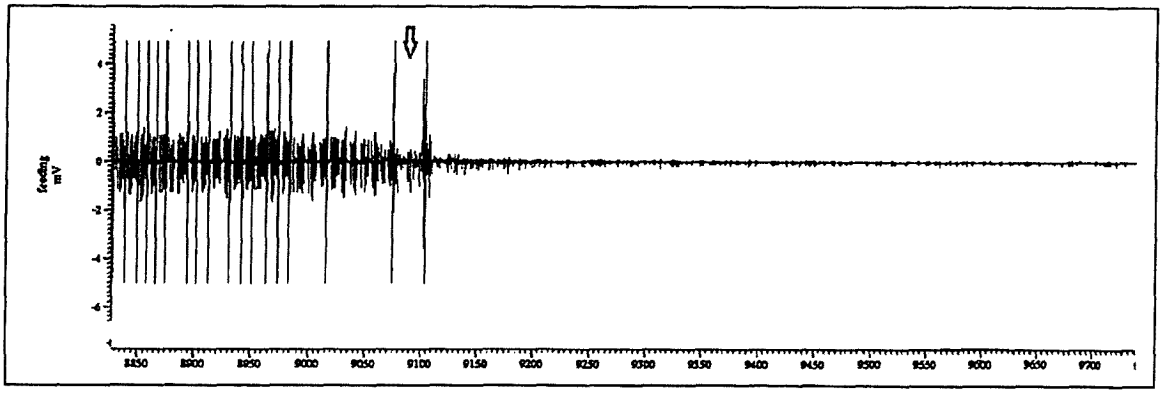


See disappearance of both ingestion- and salivation-related peaks after application of Resultix to the tick.

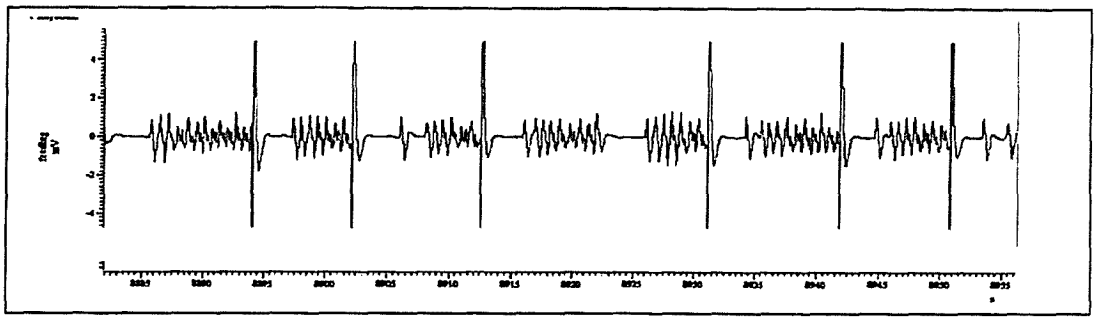


Preparation #4.

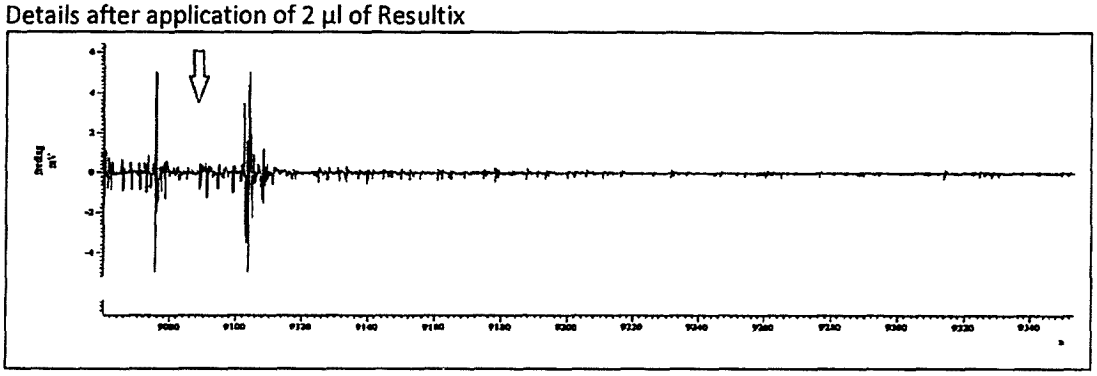
Application of 2 µl of Resultix also immediately stopped feeding activities of the 4th female fed through the capillary tube.



Details of feeding pattern before application of 2 µl of Resultix



Details after application of 2 µl of Resultix



Summary of findings from electrophysiological recordings:

Recordings directly from female ticks attached to and feeding from membrane indicate rhythmic bursting activities that associated with specific aspects of tick blood feeding. The small peaks that are associated with blood ingestion were visible in most preparations, but not visible in some preparations. However, the large units that are associated with salivation or movement of chelicerae were much more pronounced in all preparations. Results from experiments indicate that ticks attached to silicone membrane were actively sucking blood and at the same ticks actively engaged in activities essential for a blood meal, such as salivation, cheliceral movement or secreting cement to further secure attachment. In contrast, females that fed through capillary tubes demonstrated much simpler feeding patterns, which included mostly ingestion-related small peaks. There were fewer salivation or cheliceral movement related large units, suggesting blood in the capillary tube provided easy feeding conditions. Application of a volume of Resultix solution at a rate as little as 1 µl to a feeding tick (membrane or capillary tube) can immediate block blood-feeding activities in most of the preparations. Although we had observed a recovery of the blood feeding pattern after initial treatment with 1 µl of Resultix in one tick, long lasting blockage of the feeding activities were observed when ticks were treated with higher doses (2 or 4 µl). Such preparations were left to run overnight and no recovery was found. The test material (Resultix) has demonstrated the property of a fast-acting tick feeding blocker that can be potentially used to apply to ticks attached to humans or animals to immediately stop pathogen transmission and eventually kill ticks in relatively short period of time (30 – 60 min) when a very small volume (16 µl) of the material is applied to the tick.

Summary and Conclusions:

We have developed and validated a silicone membrane based tick *in vitro* feeding system to allow successful feeding of females of the lone star tick (*A. americanum*) to repletion. Compared to females that fed on live animal (cattle), females fed on the silicone membrane in the *in vitro* tick feeding system took a longer time to reach repletion, and the engorged females were smaller and laid fewer eggs. Nevertheless, the membrane feeding system has been shown in our study to be a valuable tool for evaluation of the chemical product (Resultix). It can potentially be used as a valid replacement for live animals in testing chemicals as acaricides or chemical tick remover (detachment agent) for product development and evaluation. We have demonstrated that the Piedmont product (Resultix) did not cause ticks to detach from membrane. Instead, the material killed 100% of the ticks in a short period of time (60 min) at a dose of 16 µl / tick. At 24 h post treatment, the lowest dose (0.5 µl/ tick) resulted in 83% mortality. Results of electrophysiological recording from ticks feeding on both membrane and capillary tubes have provided direct evidence that the product can immediately block tick feeding activities (blood ingestion, salivation, and cheliceral movement) at doses as low as 1 µl / tick. It is also expected that a small drop of this product applied to an attached tick would immediately stop tick feeding (and therefore pathogen transmission) and kill the ticks in minutes. It is conceivable that Resultix would cause ticks attached to a person or an animal to stop feeding immediately and die within minutes if the product is applied as approved label rate (2 sprays, 0.1 ml / spray), which is 400 times of the minimum effective dose (0.5 µl / tick) and 12.5 times of the most effective doses (16 µl / tick) we tested in this study. Results of physiological experiment indicate the possible modes of action of this product. The material killed ticks by interrupting tick respiration or gas exchange and by damaging tick cuticle that led to water loss. Although we were unable to get the blacklegged ticks (*Ixodes scapularis*) to attach to and feed on the silicone membrane, the findings we obtained from the lone star tick (*Amblyomma americanum*) should apply to the blacklegged ticks, which are smaller and perhaps more susceptible to the same chemical product (Resultix).

Abstract for Presentation at

Livestock Insect Workers Conference

July 11-14, 2015, Boston, MA

In vitro membrane feeding of the lone star tick (*Amblyomma americanum*) and its use in evaluation of acaricidal compounds

Attachment 6

Kathy Palma

From: Kathy Palma
Sent: Friday, January 08, 2016 4:03 PM
To: 'Hollis, Linda'
Cc: Bryceland.Andrew@epa.gov
Subject: Update on the Supplement to the Label for Resultix 86865-1

Importance: High

Greetings Linda,

I hope you are having a great beginning to the new year. Piedmont Animal Health (PAH) hopes that this year something can be accomplish with this request to add humans to the label of an already approved product, Resultix. Since the teleconference that was held July 1, 2015 Piedmont has not received any formal feedback from EPA as what is required to answer the questions that were raised during the discussion. Given that there has not been any constructive communication PAH is doing additional work with Dr. Li at ARS in Beltsville taking the comments that were made during the call i.e. regurgitation and repellency and designing studies to address these issues. The literature is sparse addressing regurgitation of ticks when feeding. When papers are found they are not conclusive or unanimous in the belief that regurgitation actually occurs at death while ticks are still attached. Since EPA would like to have repellency with a tick product, PAH is also investigating that possibility with this product.

I have tried to be patient but I feel that the Agency has not given any guidance other than the white papers which were informative but not relevant to what PAH needs to do to move forward with this supplement to the label. The product does as it is labeled (stops feeding immediately) and there is no denying that fact. The work was presented at a professional meeting, published and reviewed by EPA. PAH wants to do whatever needs to be done to move this project forward.

Once this final battery of investigations at ARS are complete, PAH will once again present the data for review. At that point PAH hopes a consensus can be reached.

Respectfully,

Kathy

Kathleen G. Palma, Ph.D.
Piedmont Animal Health

Attachment 8

Agency Response to

December 10, 2014

11 am- 12 pm

Meeting Minutes

Meeting Attendees:

Environmental Protection Agency (EPA)

Mr. Kevin Sweeney

Ms. Cheryl Greene

Dr. Clara Fuentes

Ms. Linda Hollis

Piedmont Animal Health (PAH)

Dr. Kathy Palma

Dr. Doug Hepler

USDA-ARS

Dr. Andrew Li

Background and Minutes

The objective of this meeting was two-fold: to discuss the findings from the in vitro feeding study conducted by Dr. Li and to determine if these data from the study could be used to amend the existing EPA label for Resultix (86865-1).

EPA RESPONSE 5/15

The evidence presented here does not support the use of the data from the study to support an amendment to the existing product label. In order to claim efficacy against ticks, 3 representative tick spp. have to be tested, including nymphs and adults. These spp. are:

Blacklegged tick (Ixodes scapularis)

Lone star tick (Ammblyoma americanum) and American dog tick (Dermacentor varialis) or Brown dog tick (Rhipicephalus sanguineus).

There is data for only one of the 3 required spp. (Amblyomma americanum). Therefore, two more spp: Blacklegged tick (Ixodes scapularis) and American dog tick (Dermacentor varialis) or Brown dog tick (Rhipicephalus sanguineus), will have to be tested. Nymph and adult stages should be tested. Nymphs of Ammblyomma americanum have not be tested.

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Tick Application on Humans under EPA Jurisdiction

The specific part of the MOU (page 4) that pertains to this topic is listed below:

l. The application of a pesticide for any of the uses listed below will be regarded solely as a pesticide usage except where it has an action described in (j), in which case it is considered to be both an animal drug and pesticide. In these cases, the agency for primary jurisdiction will be EPA.

> ***vi) Treatments that are administered topically, for control of ticks except as listed in item k.***

It is Piedmont Animal Health's understanding that the MOU, while written with reference to animal drugs, seems to draw a line between the FDA's jurisdiction and EPA's by suggesting that the latter will defer to the former if a condition exists under Section 3 subsection (k)(specific diseases) or subsection (j)(routes of administration). Resultix is not used to treat the conditions in subsection (k), so one needs to look to whether it is administered by a route specified in subsection (j). It is not.

Resultix has an anti-feeding mechanism of action on the tick. As soon as the product is applied to the tick, the tick immediately stops feeding as demonstrated in the USDA-ARS report (included). The amendment to the label for Resultix (86865-1) would include the following:

1. Add humans as another species
2. Additional claim of "once applied to the tick feeding stops immediately".
3. Resultix has treated 3 species of ticks, *R. sanguineus, D. variabilis, A. americanum* (The first 2 species were treated on dogs and cats. The third species was treated on an in-vitro feeding system.)

Based on the MOU the usage of Resultix for the topical treatment of ticks on humans should be under the primary jurisdiction of EPA.

NEXT STEPS

The proposed label amendment falls under the jurisdiction of EPA. Given that further data are needed, should Piedmont wish to continue its pursuit of the referenced amendment, we suggest an additional pre-submission meeting with BPPD to discuss specific details of the proposed label amendment and to discuss the data that will be needed.

Attachment 9

AGENDA

Date for Teleconference

September 28, 2016, 10-11 am

Piedmont Animal Health Attendees

Kathleen G. Palma, Ph.D.-Contact Person
Douglas I. Hepler, Ph.D.
Andrew Li, Ph.D., ARS Researcher

Biopesticides and Pollution Prevention Division Attendees

Clara Fuentes, Ph.D., Entomologist, Science Review
Shenell Bolden, Regulatory Action Leader, Science Review
Linda Hollis, Branch Chief
Andrew Bryceland, Biochemical Pesticides Branch, Team Leader

Meeting Background

Resultix® (86865-1) was approved August 25, 2011 as a spray to kill ticks found on cats and dogs. Since this approval Piedmont Animal Health (PAH) has been working with the Agency to amend the existing label to include humans. This product has been designated as a biopesticide with use for humans. The approved label for Resultix (included) would be amended to include humans on the label.

A protocol was submitted and reviewed in 2013. Dr. Andrew Li, an ARS researcher in Beltsville, MD incorporated some of the comments provided into the protocol. This protocol was used to collect data that was presented at a meeting held December 10, 2014. The meeting minutes submitted by email on January 16, 2015 by Piedmont Animal Health and a response from EPA written on May 5, 2015 are included. The report documenting the findings below is also included.

Findings from the Report:

The tick used in this study was *Amblyomma americanum*, the lone star tick. *Ixodes scapularis*, the blacklegged tick would not attach to the silicone membrane. The ticks were fed on a silicone membrane system where tick feeding and respiration were monitored.

safety data required? Human safety data was previously offered and not accepted for review. Does the Human Review Board have to review human data?

2. Piedmont Animal Health would like to make an additional claim on the label: "Resultix Spray kills crawling and attached ticks found on cats, dogs and humans and immediately stops tick feeding".

3. What needs to be submitted in order to amend the existing label for 86865-1?

4. How long would the amendment process take? Does this fall under PRIA?

Piedmont Animal Health has respectfully requested a meeting to discuss next steps in the label amendment process. That meeting was granted for September 28, 2016.

Contact Information:

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204 Muirs Chapel Road
Suite 200
Greensboro, NC 27410

kathy.palma@piedmontpharma.com
(b) (6) (cell)

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